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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/790,943	03/02/2004	William R. Wilson	NVT-084USRCE3	2176

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EXAMINER	
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ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/790,943	WILSON ET AL.	
	Examiner	Art Unit	
	JAMES D. ANDERSON	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,7,11,12,16 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,7,11,12,16 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Applicants' response and amendments to the claims, filed 4/21/2010, are acknowledged and entered. Claims 2 and 28 have been cancelled by Applicant. Claims 1, 3-4, 7, 11-12, 16, and 20 are pending and under examination.

Response to Arguments

Any previous rejections and/or objections to claims 2 and 28 are **withdrawn** as being moot in light of Applicant's cancellation of the claims.

Applicants' arguments, filed 4/21/2010, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112 – 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7, 11-12, 16, and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 7, the claim recites a pharmaceutical dosage comprising DMXAA or a salt thereof "in a dosage range of 500 to 4900 mg/m^2" and gemcitabine "in a ratio in the range of 1:15 to 1:10" in a mammal. The claim is unclear with regard to how much of each agent is present in the composition. The limitation, "in a dosage range of 500 to 4900 mg/m^2", does not clearly define how much DMXAA is present in the dosage form because "mg/m^2" requires that the body surface area of a subject, administration rate, and length of administration be known.

While it is acknowledged that Applicants state that a dose of 500 to 4900 mg/m^2 is suitable for *administration to a subject* with cancer in practicing the *methods* of the invention, there is no disclosure regarding how much DMXAA need be present in a *dosage form* to provide this dose range. For example, DMXAA in an amount of 100,000 mg could reasonably provide a dosage of 500 to 4900 mg/m^2 depending on at what rate the DMXAA is administered and for how long it is administered. Similarly, DMXAA in an amount of 0.001 mg could provide a dosage of 500 to 4900 mg/m^2 if it is administered over a long period of time.

Response to Arguments

Applicants argue that the claim amendments filed 4/21/2010 clearly specifies the amounts of the respective agents in the claims. Applicants' arguments and amendments to the claims have been carefully considered but they are not deemed persuasive to overcome the instant rejection. As discussed above, recitation of the dose of DMXAA in terms of "mg/m^2" in a pharmaceutical dosage form does not clearly convey how much DMXAA is present in the composition because "mg/m^2" refers to an amount of DMXAA *administered*, not how much DMXAA is present in a composition. The amount of DMXAA in the claimed compositions will differ depending not only on the body surface area of the subject intended to be administered the composition, but also on the rate and length of time DMXAA is administered. Accordingly, the metes and bounds of the claims are not clearly and unequivocally defined.

Claim Rejections - 35 USC § 112 – 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-4, 7, 11-12, 16, and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the

claimed invention. This is a written description rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1st "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001. This is a NEW MATTER rejection.

The claims recite administration of 500-4900 mg/m^2 DMXAA or a combination comprising 500 to 4900 mg/m^2 DMXAA and gemcitabine "in the range of 1:15 to 1:10" (DMXAA:gemcitabine).

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, states that Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the written description inquiry, is whatever is now claimed (see page 1117).

In the instant case, recitation of 500-4900 mg/m^2 DMXAA in conjunction with a ratio in the range of 1:15:1:10 (DMXAA:gemcitabine) introduces new matter into the claims.

Applicants claim 500-4900 mg/m^2 DMXAA and gemcitabine in a ratio range of 1:15 to 1:10 (DMXAA:gemcitabine). The claims thus encompass the following amounts of gemcitabine:

Amount of DMXAA	Ratio of DMXAA:Gemcitabine	Amount of Gemcitabine
500 mg/m^2 (claimed)	1:15 (claimed)	7500 mg/m^2 (calculated)
500 mg/m^2 (claimed)	1:10 (claimed)	5000 mg/m^2 (calculated)
4900 mg/m^2 (claimed)	1:15 (claimed)	73500 mg/m^2 (calculated)
4900 mg/m^2 (claimed)	1:10 (claimed)	49000 mg/m^2 (calculated)

As can be seen from the above table, the claims encompass administration of gemcitabine in a range of 5000 to 73500 mg/m^2. However, Applicants only disclose that the dose of gemcitabine useful in combination with DMXAA ranges from 400 to 2000 mg/m^2 (page 17, lines 6-9). **As such, the amount of gemcitabine defined in the instant claims clearly falls outside the range of gemcitabine disclosed by Applicants in the specification**.

Assuming, *arguendo*, that Applicants were to amend the claims to recite the dose of gemcitabine disclosed in the specification in conjunction with the claimed ratio, the resultant amount of DMXAA would then fall outside the range of DMXAA disclosed by Applicants.

Amount of Gemcitabine	Ratio of DMXAA:Gemcitabine	Amount of DMXAA
400 mg/m^2	1:15	26.7 mg/m^2
400 mg/m^2	1:10	40 mg/m^2
2000 mg/m^2	1:15	133.3 mg/m^2
2000 mg/m^2	1:10	200 mg/m^2

As discussed above, Applicants disclose that a suitable dose of DMXAA, for administration with, *inter alia*, an antimetabolite such as gemcitabine, is in the range of 500 to 4900 mg/m^2 (page 15, line 23 to page 16, line 9). Clearly, a dose range of 26.7 to 200 mg/m^2 of DMXAA (resulting from administration of DMXAA in a ratio of 1:15 to 1:10 when gemcitabine is administered in a range of 400 to 2000 mg/m^2) falls well outside the range of DMXAA disclosed by Applicants in the specification.

Because the instant disclosure only provides written support for: 1) 400 to 2000 mg/m^2 gemcitabine when administered with DMXAA (page 17, lines 6-9); 2) 500 to 4900 mg/m^2 DMXAA when administered with another anticancer agent such as gemcitabine (page 15, line 23 to page 16, line 9); and 3) a ratio of DMXAA to another anticancer agent of 1:100 to 1:2 (page 4, lines 17-24), the dose ranges of gemcitabine and/or DMXAA now encompassed by the claims are not supported by the disclosure. **Combining the claimed dose range of DMXAA with the claimed ratio range of 1:15 to 1:10 (DMXAA:gemcitabine) results in a dose range of gemcitabine that is not supported by the originally filed disclosure**.

There is only one example of DMXAA and gemcitabine being administered in a ratio within the claimed range of 1:15 to 1:10 (Example 2). In this example, DMXAA (20 mg/kg) and gemcitabine (240 mg/kg) were administered to mice bearing pancreatic tumors in a ratio of 1:12 (DMXAA:gemcitabine). This example only provides support for administration of 20 mg/kg DMXAA and 240 mg/kg gemcitabine to mice bearing pancreatic tumors.

Accordingly, the claims and specification do not provide written support within the meaning of 35 U.S.C. 112, 1st Paragraph for the claimed administration of 500-4900 mg/m^2 DMXAA and gemcitabine "in the range of 1:15 to 1:10" (DMXAA:gemcitabine) or the claimed combination comprising 500 to 4900 mg/m^2 DMXAA and gemcitabine "in the range of 1:15 to 1:10" (DMXAA:gemcitabine) because the DMXAA dose taken in conjunction with the claimed ratio results in a dose of gemcitabine well outside the dose range of gemcitabine disclosed in the specification as discussed *supra*.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMES D. ANDERSON whose telephone number is (571)272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/James D Anderson/
Primary Examiner, Art Unit 1614

June 22, 2010